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74. Clinical characteristics after naloxone administration in patients with confirmed methamphetamine and cocaine exposures in the Drug Overdose Toxico-Surveillance (DOTS) reporting program

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Background: Patients treated for apparent opioid overdose are increasingly found to have co-used stimulants. Naloxone adminis- tration may result in unmasked stimulant toxicity in addition to precipitated opioid withdrawal. The objective of this analysis is to determine differences in clinical symptoms post-naloxone administration among patients with methamphetamine and/or cocaine analytes in the blood (compared to those without stimulants).

Methods: The Drug Overdose Toxico-Surveillance (DOTS) report- ing program, a national network of 17 medical toxicology sites provides real-time surveillance on emergency department patients experiencing opioid or stimulant overdoses (Food and Drug Administration Contract #75F40122D00028/ 75F40123F19002). Patient interviews and chart reviews are per- formed to assess clinical characteristics (e.g., vital signs, treat- ments administered, patient response), and current/past drug use, respectively. Liquid chromatography mass spectrometry identifies and quantifies substances in patients' blood. This ana- lysis explored potential indicators of precipitated withdrawal and/or unmasked stimulant toxicity, including (1) clinician assess- ment based on the naloxone response, and/or (2) symptoms of agitation, tachycardia, vomiting, and medication administration (antiemetic, benzodiazepine, anti-psychotic) after naloxone administration. Patients were categorized into four mutually exclusive groups: no stimulants (NS); methamphetamine only (MO); cocaine only (CO); or both methamphetamine and cocaine (MC). Kruskall–Wallis tests were conducted for differences in medians, and Chi-Square and Fisher's Exact Tests were imple- mented for categorical variables. Central and site IRBs approved this study and patients provided informed consent.

Results: As of 14 March 2024, DOTS included 201 patients (36 NS cases, 78 CO cases, 63 MO cases, 24 MC cases) who had complete clinical data, full laboratory analyses, and received naloxone. Approximately half (53%) of patients received only one naloxone administration, while 27% received two naloxone administrations There were no differences in naloxone dose (in mg) or naloxone blood concentrations between categorized groups. Fentanyl was present in 89.6% of cases, 82.1% had methamphetamine and/or cocaine. The median cocaine concentration in CO cases was 2.40 (IQR: 1.90, 5.30) and MC cases was 14.00 (7.80, 37.50). The median methamphetamine concentration was 170.00 (IQR: 27.00, 335.00) in MO cases and 36.50 (12.75, 170.00) in MC cases. Xylazine was identified in 4

(6.3%) MO cases, 28 (35.9%) CO cases, and 4 (16.7%) MC cases ($p < 0.001$). Clinician-diagnosed precipitated withdrawal was more prevalent among those with- out stimulants compared to those with stimulants (data not shown, p1⁄40.006). Agitation was more common (29.2%) in MC cases (p1⁄40.05) compared with MO (6.3%), CO (10.3%), and NS (11.1%) cases.

Conclusion: Almost all patients who received naloxone in DOTS had quantified methamphetamine and/or cocaine levels. Preliminary data on patients experiencing severe/life-threatening opioid and/or stimulant overdose suggest total naloxone dosage and blood naloxone concentration levels are similar for patients with and without stimulants. Agitation was higher in patients with both methamphetamine and cocaine, but the administra- tion of medications did not differ across the groups. While these data show a preliminary evaluation of potential precipitated withdrawal and unmasked stimulant toxicity, future analyses of the growing cohort should incorporate multivariable approaches that account for quantitative values of concomitant drugs and demographics.